UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/764,676	01/26/2004	Peter Rohnert	13183.0037	9441

26712 7590 04/13/2005

HODGSON RUSS LLP
ONE M & T PLAZA
SUITE 2000
BUFFALO, NY 14203-2391

EXAMINER	
SOLOLA, TAOFIQ A	

ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 04/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,676	ROHNERT ET AL.	
	Examiner	Art Unit	
	Taofiq A. Solola	1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) 1-44 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) 1-44 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on 26 January 2004 is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Claims 1-44 are pending in this application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The structural definition of the term "prodrug" in claims 1-2, 4-5, 7, 13-15, 20-24, is not disclosed in the specification so as to determine the structures of compounds that are included and/or excluded by the term. By deleting the term the rejection would be overcome.

The phraseology the phraseology "ACE inhibitor(s)" in claims 1, 3, 5, 7, 9, 13-15, 20-24 are beyond the scope of the specification. While the phraseology embraces any compounds, known and yet and yet to be discover, that is applicable in the instant invention, the specification discloses only specific compounds. Applicant may not claim any "ACE inhibitor" compound. Applicant must claim only and "ACE inhibitor" compounds that embody applicant's invention and supported by the specification. Therefore, claims 1-44 lack adequate support in the specification. By adding the specific compounds, which have support in the specification the rejection would be overcome.

Claims 10-12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating the diseases listed in the claims, does not reasonably provide enablement for preventing the diseases. The utility is deemed speculations because it is not supported by biological assays or journal articles in the specification. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. The claimed methods of use are not believable on their face.

For rejection under 35 U.S.C. 112, first paragraph, the following factors must be considered (In re Wands, 8 USPQ2d 1400, 1404 (CAFC, 1988):

1) Breadth of claims.

2) Nature of invention.

3) State of prior art.

4) Level of ordinary skill in the art.

5) Level predictability in the art.

6) Amount of direction and guidance provided by the inventor.

7) Existence of working examples.

8) Quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breath of the claimed invention involves medicinal chemistry. The nature of the invention is in the field of using the instant compositions for preventing many disorders due to GSH deficiency. The state of the prior art is what prior art knows about the nature of the invention. There is no known prior art claiming prevention of the various disorders arising from

GSH deficiency. The level of ordinary skill in the art is high but only in using the constituents of the compositions for correcting GSH deficiency. The predictability or lack thereof in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. The lower the predictability, the higher the direction and guidance that must be provided by applicant. In the instant invention the predictability is very low and consequently, the need for higher levels of direction and guidance by applicant. However, the amount of direction and guidance provided by applicant is limited to assays comparing the effects of using the individual compounds with using them in combination. There are a very large variety of sources for the listed disorders because different mechanisms are involved. It is well known in the art that the mechanism of a specific disorder would dictate the choice of how to prevent it. Additionally, there is no evidence in the specification that established correlation between applicant's experiments and all the possible mechanisms giving rise to the various disorders. See Ex parte Mass, 9 USPQ2d 1746, 1987. Therefore, the quantity of experimentation required to use the compound as claimed, based on applicant's limited disclosure would be undue burden because, one of ordinary skill in the art would have to perform significant amount of experiments. By deleting prevention the rejection would be overcome.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1-44 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

For reasons set forth above under 35 USC 112, first paragraph, claims 1-44 are indefinite. See the Examiner's suggestions above.

Claim 1 is confusing. The composition comprises of two or more substances. The claim recites 3 major "substances" all of which have subsets of "substances". It is not clear if the claim may comprise two or more "substances" from any of the subsets. Therefore, claims 1-44 are indefinite. Appropriate correction is required.

Claim 2 is improperly depend from claim 1 for failure to limit the scope of claim 1 when all the elements of claim 1 is read into 2. Claims 4-5 are improperly depend from claim 3 for the same reason. Therefore, claims 14-15 are duplicates of claim 13, claims 18-19 are duplicates of 17, claims 22-23 are duplicates of 21, claims 26-28 are duplicates of 25, and claims 32-36 are duplicates of 31.

Claims 3-5, 7 lack proper antecedent basis in claim 1. All ACE inhibitors must be present in claim 1 while one or more may be present in claim 4-5. While two or more "substances" may be present in claim 1, only one "substance" is required in claim 7. All the constituents of claim 7 are optional because the claim 7 recites 'and/or" between the constituents. For the same reason, claims 20-24 lack proper antecedent basis in claims 2-6 respectively.

Claims 8 and 9 are duplicates because route of administration is inherent in the type of formulation or composition. For the same reason, claims 31-36 are duplicates of claims 25-30.

Claims 8, 25-30 each recites "buccal", "oral", "pulmonal", and "nasal". This render the claims confusing since buccal cavity means mouth. Also pulmonal and nasal are synonymous.

Claims 10-12, 37-44 are drawn to methods of using the instant compositions without indication as to whether they are use in cell tissue culture, a patient having the a relevant disease or administration thereof. Therefore, the claims are indefinite.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-6, 16-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gillissen et al., Respiratory Med. (1998), Vol. 92, pages 609-623, further in view of Derick et al., Biochem. Biophy. Research Comm. (1995), Vol. 207, No. 1, pages 258-264, and Elena et al., Am. J. Physiol. Regulatory Integrative Comp. Physiol., (2000), Vol. 278, pages R572-R577.

Applicant claims a medicament (composition) comprising ambroxile and α-lipoic acid and Angiotesin-converting enzyme inhibitor (ACE inhibitor) for correcting a disturbance of thiol-disulfide status (correcting GSH deficiency). In preferred embodiment applicant claims several dosages, types of composition, routes of administration and treatment of disorders arising from GSH deficiency.

Determination of the scope and content of the prior art (MPEP ∋2141.01

Gillissen et al., teach a composition comprising ambroxile as anti-oxidant therapy (correcting GSH deficiency). Derick et al., teach a composition comprising α-lipoic acid for

increasing intracellular GSH. Elena et al., teach a composition comprising enalapril or captopril for enhancing GSH-dependent anti-oxidant defenses (correcting a disturbance of thiol-disulfide status or GSH deficiency).

Ascertainment of the difference between the prior art and the claims (MPEP ∋2141.02)

The difference between the instant invention and that of Gillissen et al., and Derick et al., is that applicant claims a composition comprising one or more of ambroxile, ACE inhibitor(s) and α-lipoic acid instead of a composition comprising ambroxile by Gillissen et al., and a composition comprising α-lipoic acid by Derick et al., and a composition comprising enalapril or captopril by Elena et al. Applicant also claims several dosages, types of composition, routes of administration and treatment of disorders arising from GSH deficiency.

Finding of prima facie obviousness--rational and motivation (MPEP ∋2142.2413)

The combination of compounds for a certain function where the compounds are known to perform the function individually is prima facie obvious. *In re Kerkhoven,* 205 USPQ 1069 (1980). Therefore, the instant invention is prima facie obvious from the teachings of Gillissen et al., Derick et al., and Elena et al. Claiming dosages, types of composition, routes of administration and treatment of disorders arising from GSH deficiency is not patentable significant because they do not rise to the level of invention under US patent practice. Knowing that ambroxile, α-lipoic acid and ACE inhibitors, individually, are useful for correcting GSH deficiency, one of ordinary skill in the art would have known to use them individually or combine them in a composition for correcting GSH deficiency. The motivation to combine them is from the teachings of Gillissen et al., Derick et al., and Elena et al., that ambroxile, α-lipoic

acid, and enalapril or captopril, respectively are useful for correcting GSH deficiency, and from the common practice in medicine of using cocktail medication to improve patient recovery.

Applicant should note that correcting GSH deficiency with a compound and treating diseases arising from GSH deficiency with the compound are not patentable distinct under US patent practice. Applicant should also note that intended use is not a limitation in a compound or composition claim. *In re Hack,* 114USPQ 161 (CCPA, 1957); *In re Craig,* 90 USPQ 33 (CCPA, 1951); *In re Brenner,* 82 USPQ 49 (CCPA, 1949).

Double Patenting

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 7, 20-24, 30, 36 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 18-23 of copending Application No.10/478,174, and claims 1-18 of co-pending application 10/479,080. The cited claims in the these applications are drawn to the same subject matter. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Claims 37-44 are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims 24-28 of copending Application No.10/478,174. The cited claims in

the these applications are drawn to the same subject matter. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Abstract

The abstract is objected to for being too long. Appropriate correction is required.

Telephone Inquiry

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Taofiq A. Solola, PhD, JD, whose telephone number is (571) 272-0709.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Joseph McKane, can be reached on (571) 272-0699. The fax phone number for this Group is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Solola

TAOFIQ SOLOLA
PRIMARY EXAMINER
Group 1626

April 7, 2005